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Paper NO. 13
DJS 11/14/01

RAW SEQUENCE LISTING

PATENT APPLICATION: US/09/308,080

DATE: 10/10/2001

TIME: 10:36:47

13

Input Set : A:\Nih271-1.app

Output Set: N:\CRF3\10102001\I308080.raw

ENTERED

SEQUENCE LISTING

4 (1) GENERAL INFORMATION:

6 (i) APPLICANT: Gonzalez, Frank J.

7 Fernandez-Salguero, Pedro

9 (ii) TITLE OF INVENTION: Methods and Compositions for Detecting

10 Dihydropyrimidine Dehydrogenase Splicing Mutations

12 (iii) NUMBER OF SEQUENCES: 7

14 (iv) CORRESPONDENCE ADDRESS:

15 (A) ADDRESSEE: Townsend and Townsend and Crew LLP

16 (B) STREET: Two Embarcadero Center, Eighth Floor

17 (C) CITY: San Francisco

18 (D) STATE: California

19 (E) COUNTRY: USA

20 (F) ZIP: 94111-3834

22 (v) COMPUTER READABLE FORM:

23 (A) MEDIUM TYPE: Floppy disk

24 (B) COMPUTER: IBM PC compatible

25 (C) OPERATING SYSTEM: PC-DOS/MS-DOS

26 (D) SOFTWARE: PatentIn Release #1.0, Version #1.30

28 (vi) CURRENT APPLICATION DATA:

C--> 29 (A) APPLICATION NUMBER: US/09/308,080

C--> 30 (B) FILING DATE: 28-Oct-1999

31 (C) CLASSIFICATION:

37 (vii) PRIOR APPLICATION DATA:

34 (A) APPLICATION NUMBER: US 60/013,835

35 (B) FILING DATE: 20-MAR-1996

38 (A) APPLICATION NUMBER: WO PCT/US97/04269

39 (B) FILING DATE: 19-MAR-1997

41 (viii) ATTORNEY/AGENT INFORMATION:

42 (A) NAME: Weber, Kenneth A.

43 (B) REGISTRATION NUMBER: 31,677

44 (C) REFERENCE/DOCKET NUMBER: 015280-271100US

46 (ix) TELECOMMUNICATION INFORMATION:

47 (A) TELEPHONE: (415) 576-0200

48 (B) TELEFAX: (415) 576-0300

51 (2) INFORMATION FOR SEQ ID NO: 1:

53 (i) SEQUENCE CHARACTERISTICS:

54 (A) LENGTH: 861 base pairs

55 (B) TYPE: nucleic acid

56 (C) STRANDEDNESS: single

57 (D) TOPOLOGY: linear

59 (ii) MOLECULE TYPE: DNA (genomic)

62 (ix) FEATURE:

63 (A) NAME/KEY: CDS

64 (B) LOCATION: 269..433

65 (D) OTHER INFORMATION: /note= "dihydropyrimidine dehydrogenase

66 (DPD) gene region of splicing mutant

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67 mRNA encoding amino acids 581-635"

69 (ix) FEATURE:

70 (A) NAME/KEY: mutation

71 (B) LOCATION: replace(434, "a")

72 (D) OTHER INFORMATION: /note= "G -> A mutation at 3' donor

73 splice junction consensus sequence

74 leading to loss of exon in DPD mRNA

75 and DPD deficiency"

78 (xi) SEQUENCE DESCRIPTION: SEQ ID NO: 1:

```

80 TGTTAATGAA GATAAATATT TTTGTTTTTT CGCTGTTCTA AACCTAGGGT TACAAGAAGT      60
82 AATTTATCTG GAGCTAACAA ATACTTTATT TTACCTTTTT ATTTGCAAGT AGTTTATGTT      120
84 CAATTCTAAT TTAATGTATA TTAATAATTC CTCTGCAAAT ATGTGAGGAG GGACCTCATA      180
86 AAATATTGTC ATATGGAAAT GAGCAGATAA TAAAGATTAT AGCTTTTCTT TGTCAAAAGG      240
88 AGACTCAATA TCTTTACTCT TTCATGAG GAC ATT GTG ACA AAT GTT TCC CCC      292
89                                     Asp Ile Val Thr Asn Val Ser Pro
90                                     1           5
92 ATA ATC ATC CGG GGA ACC ACC TCT GGC CCC ATG TAT GGC CCT GGA CAA      340
93 Ile Ile Ile Arg Gly Thr Thr Ser Gly Pro Met Tyr Gly Pro Gly Gln
94      10           15           20
96 AGC TCC TTT CTG AAT ATT GAG CTC ATC AGT GAG AAA ACG GCT GCA TAT      388
97 Ser Ser Phe Leu Asn Ile Glu Leu Ile Ser Glu Lys Thr Ala Ala Tyr
98      25           30           35           40
100 TGG TGT CAA AGT GTC ACT GAA CTA AAG GCT GAC TTC CCA GAC AAC      433
101 Trp Cys Gln Ser Val Thr Glu Leu Lys Ala Asp Phe Pro Asp Asn
102      45           50           55
104 GTAAGTGTGA TAAAAATCTA AAACAAGAGA ATTGGCATAA GTTGGTGAAT GTTTATTTAA      493
106 ACATCCAATT CATAGGCTTA TAAATATTAA TGTGTATATT TTATCAACGA ATCTGCCAGT      553
108 TGCTTTGCTG ATGCATAGAA AGATAAAAAA GAAAGAAAAG CTCAAGAACT CATAAAAACC      613
110 CACACAATGT GAAGCTCTGT TATAAATGGG TGCCATGTAA GATGGAAGAA GTATCTACAT      673
112 AAGCAGAAGG AAGAGAAATG AAATACTCAT TTTATTGAGT TGGCCCCCAC TGTATGTGGC      733
114 TGGTATTTAT GAAGGTGATG ACCCAGGAAG AAATTGTAAA CTATAAACCA CTCCAAATAT      793
116 AAACCCGAGG CAGAAGCAGC ATATCTCCTA TGAAGCCTGT ATTTACTCAG TGGGAAATAA      853
118 TTTATTTAA                                     861

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121 (2) INFORMATION FOR SEQ ID NO: 2:

123 (i) SEQUENCE CHARACTERISTICS:

124 (A) LENGTH: 55 amino acids

125 (B) TYPE: amino acid

126 (D) TOPOLOGY: linear

128 (ii) MOLECULE TYPE: protein

130 (xi) SEQUENCE DESCRIPTION: SEQ ID NO: 2:

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132 Asp Ile Val Thr Asn Val Ser Pro Ile Ile Ile Arg Gly Thr Thr Ser
133      1           5           10           15
135 Gly Pro Met Tyr Gly Pro Gly Gln Ser Ser Phe Leu Asn Ile Glu Leu
136      20           25           30
138 Ile Ser Glu Lys Thr Ala Ala Tyr Trp Cys Gln Ser Val Thr Glu Leu
139      35           40           45
141 Lys Ala Asp Phe Pro Asp Asn
142      50           55
145 (2) INFORMATION FOR SEQ ID NO: 3:

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147      (i) SEQUENCE CHARACTERISTICS:
148          (A) LENGTH: 22 base pairs
149          (B) TYPE: nucleic acid
150          (C) STRANDEDNESS: single
151          (D) TOPOLOGY: linear
W--> 153      (ii) MOLECULE TYPE: DNA
154      (ix) FEATURE:
155          (A) NAME/KEY: -
156          (B) LOCATION: 1..22
157          (D) OTHER INFORMATION: /note= "primer DELF1 (forward)"
162      (xi) SEQUENCE DESCRIPTION: SEQ ID NO: 3:
164 TGCAAAATATG TGAGGAGGGA CC                                     22
167 (2) INFORMATION FOR SEQ ID NO: 4:
169      (i) SEQUENCE CHARACTERISTICS:
170          (A) LENGTH: 22 base pairs
171          (B) TYPE: nucleic acid
172          (C) STRANDEDNESS: single
173          (D) TOPOLOGY: linear
W--> 175      (ii) MOLECULE TYPE: DNA
176      (ix) FEATURE:
177          (A) NAME/KEY: -
178          (B) LOCATION: 1..22
179          (D) OTHER INFORMATION: /note= "primer DELR1 (reverse)"
184      (xi) SEQUENCE DESCRIPTION: SEQ ID NO: 4:
186 CAGCAAAGCA ACTGGCAGAT TC                                     22
189 (2) INFORMATION FOR SEQ ID NO: 5:
191      (i) SEQUENCE CHARACTERISTICS:
192          (A) LENGTH: 18 base pairs
193          (B) TYPE: nucleic acid
194          (C) STRANDEDNESS: single
195          (D) TOPOLOGY: linear
W--> 197      (ii) MOLECULE TYPE: DNA
198      (ix) FEATURE:
199          (A) NAME/KEY: -
200          (B) LOCATION: 1..18
201          (D) OTHER INFORMATION: /note= "primer DPD15F (forward)"
206      (xi) SEQUENCE DESCRIPTION: SEQ ID NO: 5:
208 TTGTGACAAA TGTTTCCC                                     18
211 (2) INFORMATION FOR SEQ ID NO: 6:
213      (i) SEQUENCE CHARACTERISTICS:
214          (A) LENGTH: 24 base pairs
215          (B) TYPE: nucleic acid
216          (C) STRANDEDNESS: single
217          (D) TOPOLOGY: linear
W--> 219      (ii) MOLECULE TYPE: DNA
220      (ix) FEATURE:
221          (A) NAME/KEY: -
222          (B) LOCATION: 1..24
223          (D) OTHER INFORMATION: /note= "primer DPD15R (reverse)"

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Input Set : A:\Nih271-1.app

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228      (xi) SEQUENCE DESCRIPTION: SEQ ID NO: 6:
230 AGTCAGCCTT TAGTTCAGTG ACAC                                24
233 (2) INFORMATION FOR SEQ ID NO: 7:
235      (i) SEQUENCE CHARACTERISTICS:
236          (A) LENGTH: 856 base pairs
237          (B) TYPE: nucleic acid
238          (C) STRANDEDNESS: single
239          (D) TOPOLOGY: linear
W--> 241      (ii) MOLECULE TYPE: DNA
244      (xi) SEQUENCE DESCRIPTION: SEQ ID NO: 7:
246 TGTTAATGAA GATAAATATT TTTATTTTTG CGCTATTCTA AACCTAGAGT TACAAGAAGT        60
248 AATTTATCTG GAGCTAACAA ATACTTTATT TTACCTTTTT ATTTGCAAGT AGTTTATGTT        120
250 CAATTCTAAT TTAATGTATA TTAAAAATTC CTCTGCAAAT ATGTGAGGAG GGACCTCATA        180
252 AAATATTGTC ATATGGAGAT GAGCAGATAA TAAAGATTAT AGCTTTTCTT TGTCAAAAGG        240
254 AGACTCAATA TCTTTACTCT TTCATCAGGA CATTGTGACA AATGTTTCCC CCATAATCAT        300
256 CCGGGGAACC ACCTCTGGCC CCATGTATGG CCCTGGACAA AGCTCCTTTC TGAATATTGA        360
258 GCTCATCAGT GAGAAAACGG CTGCATATTG GTGTCAAAGT GTCAGTGAAC TAAAGGCTGA        420
260 CTTCCCAGAC AACGTAAGTG TGATAAAAAAT CTAAAACAAG AGAATTGGCA TAAGTTGGTG        480
262 AATGTTTATT TAAACATCCA ATTCATAGGC TTATAAATAT TAATGTGTAT ATTTTATCAA        540
264 AGAATCTGCC AGTTGCTTTG CTGATGCATA GAAAGATAAA AAAGAAAGAA AAGCTCAAGA        600
266 ACTCATAAAA ACCCACACAA TGTGAAGCTC GTTATAAATG GGTGCCATGT AAGATGGAAG        660
268 AAGTATCTAC ATAAGCAGAA GGAAGAGAAA TGAAATACTC AATTTATTGA GTTGGCCCCC        720
270 ACTGTATGTG GCTGGCATT TGAAGGTGA TGACCCAGGA AGAAATTGTC ACCTATAAAT        780
272 CATCCAAATA TCCCGAGGCA GAAGCAGCAT CTCTCCTATG AAGTCTGTAT TTATTTTCAGC        840
274 GGGAAATAAT TTATTA                                          856

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VERIFICATION SUMMARY

DATE: 10/10/2001

PATENT APPLICATION: US/09/308,080

TIME: 10:36:48

Input Set : A:\Nih271-1.app

Output Set: N:\CRF3\10102001\I308080.raw

L:29 M:220 C: Keyword misspelled or invalid format, [(A) APPLICATION NUMBER:]
L:30 M:220 C: Keyword misspelled or invalid format, [(B) FILING DATE:]
L:153 M:246 W: Invalid value of Alpha Sequence Header Field, [MOLECULE TYPE:], SeqNo=3
L:175 M:246 W: Invalid value of Alpha Sequence Header Field, [MOLECULE TYPE:], SeqNo=4
L:197 M:246 W: Invalid value of Alpha Sequence Header Field, [MOLECULE TYPE:], SeqNo=5
L:219 M:246 W: Invalid value of Alpha Sequence Header Field, [MOLECULE TYPE:], SeqNo=6
L:241 M:246 W: Invalid value of Alpha Sequence Header Field, [MOLECULE TYPE:], SeqNo=7